Learning Objectives:

Introduction: Cisplatin (CDDP) is a widely used chemotherapeutic drug with important side-effects, such as ototoxicity. CDDP ototoxicity affects individuals variably, which is mostly due to individual genetic factors. Aim of this study is to analyse the genetic background of the patients in which severe ototoxicity occurred.

Methods: 72 children who received CDDP chemotherapy between January 2013 and March 2015 were included in the study. Audiological evaluations were performed before and minimum three months after the therapy. Ototoxicity was evaluated using Muenster, Brock classifications. During routine controls, 5cc of peripheral blood samples were taken into EDTA-coated tubes. Peripheric blood mononuclear cell and subsequent DNA isolations were performed. In order to analyze the genetic background of patients, we performed comparative genomic hybridization (CGH) arrays for 5 patients with the most severe ototoxicity (Grade 3 and 4), among the studied 72 patients. Results were evaluated statistically by using “Agilent Cytogenomics Software”.

Results: CGH analysis showed some common genetic differences among evaluated patients. Chr8.p23.1 (Defensin-family genes) deletion was seen in 3 patients. Chr11.q13.2 (NDUFV1) gain was observed among 4 patients. Chr14.q32.33 (ADAM6) amplification, Chr2.p21 (SIX3) amplification and Chr11.p15.5 (H19) gain were common in all patients. Chr20.q13.32 (GNAS) gain was also seen in 3 patients and this chromosomal region was deleted in one patient. Further assessments may be important to understand the roles of these genes in CDDP induced ototoxicity.

Conclusion: In order to minimize the risk for CDDP ototoxicity, identification of genetic differences is of great importance. Further studies on new candidate genes such as Defensin-family genes, ADAM6, SIX3, GNAS, NDUFV1, and H19 should be performed to better understand their effect on CDDP ototoxicity.